This manual was published thanks to financial support from:

The Association Française Raoul Follereau (AFRF), France is an NGO dedicated to leprosy control in 31 countries worldwide. It also supports six research projects on leprosy, including the genome sequencing of Mycobacterium leprae. Long before the first International Conference on Buruli Ulcer Control and Research, Yamoussoukro, Côte d’Ivoire, 1998, AFRF had taken up the new challenge of the health and social problems caused by Buruli ulcer, working in Benin and Côte d’Ivoire since 1996. The Association also provides financial assistance to research activities on the genome sequencing of Mycobacterium ulcerans and on the drug treatment of the disease. It is now considering supporting other countries, starting with Ghana. AFRF is committed to mobilizing the international support needed to meet the challenges posed by Buruli ulcer.

For more information, visit the AFRF website: http://www.raoul-follereau.org

ANESVAD, Spain is an NGO that has been working against leprosy and implementing health, social and educational projects in 28 of the poorest developing countries for over 30 years. Currently it counts on the support of over 135 000 partners and collaborators in Spain. It has recently begun work on Buruli ulcer in Côte d’Ivoire, carrying out programmes to detect the disease at an early stage and undertaking prevention, surgical treatment, training of specialized medical staff and social awareness campaigns, with the aim of limiting the impact of Buruli ulcer.

For more information, visit the ANESVAD website: http://www.anesvad.org

Médecins Sans Frontières (MSF) is an international humanitarian aid organization that provides emergency medical assistance to populations in danger in more than 80 countries. MSF Luxembourg has been involved in Buruli ulcer control activities in Benin since 1997. MSF has upgraded the Lalo Health Centre with surgical and laboratory facilities to improve the care of patients. Apart from surgical activities, other key activities include health education in affected communities, case-finding and training of health care providers, teachers and traditional healers. In terms of Buruli ulcer research, MSF is collaborating with the Institute of Tropical Medicine, Antwerp, Belgium.

For more information, visit the MSF Luxembourg’s website at: http://www.msf.lu

The Nippon Foundation, Japan is a private grant-making foundation whose activities cover social welfare, public health, volunteer support and overseas assistance. Since 1975 it has been working through the Sasakawa Memorial Health Foundation to aid WHO in its fight to eliminate leprosy. Starting in 1998, The Nippon Foundation also began providing financial support to the WHO Global Buruli Ulcer Initiative. The Foundation, in tandem with WHO and several academic institutions, is currently exploring options for improved surgical management of the disease. Finally, it is also collaborating with WHO, AFRF and other partners to find a drug treatment for Buruli ulcer.

For more information, visit The Nippon Foundation’s website at: http://www.nippon-foundation.or.jp
Buruli Ulcer

Management of Mycobacterium ulcerans disease

A MANUAL FOR HEALTH CARE PROVIDERS

EDITED BY:

DOCTOR JOHN BUNTINE
Cornell Specialists’ Centre
Camberwell, Victoria, Australia

DOCTOR KIMBALL CROFTS
Plastic Surgery Institute of Utah
Provo, Utah, United States of America

World Health Organization
Acknowledgements

With special thanks to: George Amofah, Ministry of Health, Ghana • Kwame Asamoa, Ministry of Health, Ghana • David Ashford, CDC, Atlanta, USA • Rosemary Bell, France • Samuel Etuaful, St Martin’s Catholic Hospital, Agroyesum, Ghana • Sister Joseph, Wewak General Hospital, Papua New Guinea • Luca Saguatti, Italy, for their support
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Contributors

Dr Pius Agbenorku, Department of Plastic Surgery, Komfo Anokye Teaching Hospital, Kumasi, Ghana / Sister Julia Aguiar, Mission Catholique Zagnanado, Zagnanado, Benin / Prof. Henri Assé, Institute Raoul Follereau, Adzope, Côte d’Ivoire / Dr John Buntine, Cornell Specialists’ Centre, Camberwell, Victoria, Australia / Dr Kimball Crofts, HART USA / Dr Afua Hesse, Department of Pediatric Surgery, Korle-Bu Teaching Hospital, Accra, Ghana / Sister Joseph, Wewak Hospital, Wewak, East Sepik Province, Papua New Guinea / Prof. Christophe Oberlin, Service de Chirurgie orthopédique et traumatologique, Groupe Hospitalier Bichat Claude-Bernard, Paris, France / Dr G. Battista Priuli, Hôpital St-Jean-de-Dieu, Tanguêta, Benin / Mrs May Smith, Mossman District Hospital, Cairns, Australia / Dr Christina Steffen, Cairns Base Hospital, Cairns, Australia / Dr Kingsley Asiedu, Communicable Diseases Control, Prevention and Eradication, World Health Organization, Geneva, Switzerland / Mr Anders Eklund, Disability and Rehabilitation, Non–communicable Diseases and Mental Health, World Health Organization, Geneva, Switzerland / Dr Ann Goerd, Disability and Rehabilitation, Noncommunicable Diseases and Mental Health, World Health Organization, Geneva, Switzerland / Dr Jean Emmanuel, Blood Safety and Clinical Technology, Health Technology and Pharmaceuticals, World Health Organization, Geneva, Switzerland
Preface

This manual is addressed to health care providers dealing with Mycobacterium ulcerans disease (Buruli ulcer). The manual aims to achieve a better understanding of the disease, its clinical presentation and its surgical management. The manual is aimed particularly at district health care providers. A comprehensive protocol, adapted to each form and stage of the disease, is presented together with comments on the levels of resources and capabilities necessary to shorten the length of treatment, to prevent complications and to minimize undesired sequela and thus to obtain the best possible outcome for each patient. Some sections include advice relevant to surgeons (e.g. relating to bone infection). However, the level to which particular comments are intended to apply should be clear from the context.

Please note: This manual is not intended to set down a standard of medical care. It is not a replacement for medical and paramedical textbooks. Adherence to the advice given will not ensure a successful outcome in every case. The manual should not be construed as including all proper methods of care or as excluding other methods of care. Ultimate judgement regarding a particular surgical procedure or treatment must be made by the involved health care provider consistent with the clinical presentation of the patient and the options available for diagnosis and treatment.
Illustrations

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In 1998, the World Health Organization (WHO) established the Global Buruli Ulcer Initiative (GBUI) in response to the growing spread and impact of Buruli ulcer, Mycobacterium ulcerans disease. The disease exists or has been suspected in at least 31 countries (Fig. 1). The primary objectives of the GBUI are: to raise awareness of the disease, to mobilize support for affected countries, to promote and to coordinate research activities and to coordinate the work of nongovernmental organizations (NGOs) and other partners. A summary of the achievements of the GBUI is presented in Annex 5.

In 1897, Sir Albert Cook in Uganda described skin ulcers consistent with Buruli ulcer but he did not publish these cases in the medical literature. In 1948, MacCallum et al. published the first confirmed cases of the disease. These patients were in Australia. The disease was called Bairnsdale ulcer after the main town in the original endemic region. In south-eastern Australia, the disease is still often referred to as Bairnsdale ulcer but, in parts of Africa, it is called “Buruli ulcer”, the name coming from a county in Uganda where large numbers of cases were reported in the 1950s.

It is called “Buruli ulcer”, the name coming from a county in Uganda where cases were reported in the 1950s.
Epidemiology and transmission

After tuberculosis and leprosy, Buruli ulcer is the most common mycobacterial infection of humans. It is caused by Mycobacterium ulcerans. The disease often occurs in people who live or work close to rivers and stagnant bodies of water. Changes in the environment, such as the construction of irrigation systems and dams, seem to have played a role in the resurgence of the disease. The mode of transmission is not known, but recent evidence suggests that aquatic insects (Naucoris and Dyplonychus species) may be involved. Trauma to contaminated skin sites appears to be the means by which the organism enters the body. There is little proven evidence of transmission from person to person. No racial or social group is exempt. Infection with the human immunodeficiency virus (HIV) is not a known risk factor. The disease is more severe in impoverished inhabitants of remote rural areas. About 70% of those affected are children under the age of 15 years. Mortality due to the disease is low, but morbidity is high. Complications include contracture deformities, amputation of limbs, and involvement of the eye, breast and genitalia. In some localities 20–25% of those with healed lesions are left with disabilities that have a long-term social and economic impact. The current economic and social burden imposed by Buruli ulcer is enormous. In Ghana, the average cost of treatment per patient is estimated to be US$ 780.

The causative organism

Mycobacterium ulcerans is a slow growing environmental mycobacterium. It is an acid-fast micro-organism that grows on common mycobacteriological media, e.g. Löwenstein-Jensen (L-J) medium. It grows best at low temperatures (30–32 °C), at lower than atmospheric oxygen tension (pO$_2$ < 2.5 kPa) and within a pH range of 5.4–7.4. A positive culture requires incubation for 6 to 8 weeks (or longer) under appropriate conditions.

Toxin

A toxin that causes tissue necrosis has been known for some time. Recently, one such compound—a polyketide-derived macrolide called mycolactone—has been identified and its chemical structure established. The toxin has both cytotoxic and local immunosuppressive properties. Injection of the purified toxin into experimental animals causes changes in subcutaneous fat similar to those seen in Buruli ulcers. This is the first macrolide known to be produced by a human pathogen and the only macrolide identified in the genus Mycobacterium.
Pathogenesis
Once introduced into the subcutaneous tissue the organism proliferates and elaborates a toxin that has affinity for fat cells. The resulting necrosis then provides a favourable milieu for further proliferation of the organism. During the necrotic phase, there is very little or no cellular immune response and the burulin skin test is negative. By an unknown mechanism, either the toxin may be neutralized or the organism may cease to proliferate or to produce toxin. Healing seems to begin when the host develops cell-mediated immunity, at which time the burulin skin test may become positive. The inflammatory cells then destroy the etiological agent (M. ulcerans) and the disease subsides with scarring. Bones may be affected by direct spread from the lesion or as a result of M. ulcerans bacteraemia. In contrast to other pathogenic mycobacteria, which are facultative intracellular parasites of macrophages, M. ulcerans occurs primarily as extracellular microcolonies.

Clinical spectrum of the disease
Clinically the disease manifests as papules, nodules, plaques, oedematous forms and ulcers. The disease may be active (ongoing infection) or inactive (previous infection with characteristic depressed stellate scars with or without other sequelae). A new case is a patient with no previous history of or treatment for Buruli ulcer. A recurrent case is a patient presenting within one year with a further lesion at the same or a different site. Recurrence rates vary from 16% for patients presenting early to 28% for patients presenting late. Recurrence at the same site may be due to inadequate excision. Recurrence at a different site may be due to haematogenous or lymphatic spread.

Diagnosis
Clinical: In a known endemic area, an experienced person can make the diagnosis of Buruli ulcer on clinical grounds. The following clinico-epidemiological features are important diagnostic clues:
1) the patient lives in or has travelled to a known endemic area;
2) most patients are children under 15 years of age;
3) about 85% of lesions are on the limbs;
4) lower limb lesions are twice as common as upper limb lesions.

Laboratory: Any two of the following findings are required to positively diagnose Buruli ulcers:
1) acid-fast bacilli in a smear stained by the Ziehl-Neelsen (ZN) technique;
2) positive culture of M. ulcerans (but this requires 6–8 weeks or longer);
3) histopathological study of excisional biopsy specimen (result available rapidly);
4) positive polymerase chain reaction (PCR) for DNA from M. ulcerans.

Treatment
Drug treatment: Several antimycobacterial agents have in vitro activity against the causative organism but no single agent has been proven to be regularly useful in the treatment of the disease. Agents used include rifampicin, rifabutin, clarithromycin, azithromycin, streptomycin and amikacin. Combinations of agents have been used, with apparently varying success. Drug treatment alone, even with combinations of drugs, is usually ineffective when there is an established, progressing lesion. Research into drug treatment is a priority.
Surgical treatment: This is accepted as the current definitive treatment. Limiting factors include:
1) inadequate surgical facilities;
2) need for prolonged stay in hospital;
3) high treatment costs;
4) recurrence after surgical treatment (rates of 16% to 28%);
5) the risk of transmission of infections such as HIV.
Other adjuncts to treatment include heat and hyperbaric oxygen, which have not been definitively proven and may be impractical in developing countries.

Control and prevention
Community control strategies are currently limited by a lack of knowledge regarding the source of infection and the mode of transmission. The current standard treatment is surgery. Expert opinion is that early surgical management leads to improved results and resolution that are both cost saving. Early treatment is best promoted by an effective village-based surveillance programme. Current attitudes and beliefs may stigmatize and create fear in the affected individuals thereby delaying early and effective treatment. Educational materials should dispel such misinformation and focus on early detection and surgery. Minor surgery (e.g., nodulectomies) may be performed at the local level.

What you should do
The current control strategy promoted by the Global Buruli Ulcer Initiative consists of:
• health education and staff training in the communities most affected;
• strengthening the health care capacity in endemic areas by upgrading surgical facilities, ensuring adequate treatment supplies and improving laboratories;
• surgical training to enable other health workers (e.g. nurses, medical assistants) to perform effective minor surgery;
• community-based surveillance to improve early detection and rapid referral for treatment in collaboration with disease control programmes such as those for leprosy and dracunculiasis;
• adoption of educational material adapted to the needs of each country;
• developing successful motivational strategies;
• rehabilitation of those already deformed by the disease.

Key points
1) About 70% of those infected with Buruli ulcer are children under 15 years old.
2) In Ghana the average cost to treat Buruli ulcer is over US$ 780 per person.
3) The accepted current treatment for Buruli ulcer is usually surgery.
Clinical diagnosis

Chapter 1

Non-ulcerative forms I Ulcerative forms I Bone involvement I Complications and sequelae I Differential diagnosis
Clinical diagnosis

Objectives
This chapter will assist you to recognize different forms of Mycobacterium ulcerans disease and to diagnose the condition irrespective of the stage at which it presents.

What you should know
Always consider the diagnosis of Mycobacterium ulcerans disease in patients who live in an endemic area. There are basically two presentations of M. ulcerans disease: non-ulcerative and ulcerative. Non-ulcerative forms present as:

<table>
<thead>
<tr>
<th>Non-ulcerative forms</th>
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<tbody>
<tr>
<td>Papule</td>
</tr>
<tr>
<td>Nodule</td>
</tr>
<tr>
<td>Plaque</td>
</tr>
<tr>
<td>Oedematous forms</td>
</tr>
</tbody>
</table>

1. **Non-ulcerative forms**

   - **Papule:** This is defined as a painless, raised skin lesion, less than 1 cm in diameter. The surrounding skin is reddened (Fig. 2). This form is commonly seen in Australia.

   - **Nodule:** A nodule is a lesion that extends from the skin into the subcutaneous tissue. It is 1–2 cm in diameter. It is usually painless but may be itchy and the surrounding skin may be discoloured compared to adjacent areas (Fig. 3). This form is commonly seen in Africa.

   - **Plaque:** This is a firm, painless, elevated, well-demarcated lesion more than 2 cm in diameter with irregular edges. The skin over the lesion is often reddened or otherwise discoloured (Fig. 4).

   - **Oedematous form:** There is a diffuse, extensive, usually non-pitting swelling. The affected area has ill-defined margins, is firm and painless and involves part or all of a limb or other part of the body. There may be colour changes over the affected region (Fig. 5a–b) and the disease may be accompanied by fever.
2 Ulcerative forms

When fully developed, the ulcer has undermined edges and is indurated peripherally. The floor of the ulcer may have a white cotton wool-like appearance from the necrotic slough (Fig. 6a–d).

The ulcer is usually painless, unless there is secondary bacterial infection. When there is more than one ulcer and the ulcers are close together, they often communicate beneath intact skin.
Bone involvement

- **Osteomyelitis:** This is true osteomyelitis. It may be focal or multifocal. The overlying skin is often intact with no obvious lesion. Osteomyelitis may occur as a primary condition or as a metastatic condition, sometimes at a distance from a cutaneous lesion(s) or after a cutaneous lesion has healed.

Mycobacterium ulcerans osteomyelitis is initially painless, but subsequently frankly painful, and well localized. There is usually an identifiable area of increased warmth. A swelling then appears and this may progress to a fistula which discharges necrotic material. Incision of the swelling reveals gelatinous tissue and, beneath this, the bone has a moth-eaten appearance. Unlike open (contiguous) osteitis, the bone is the site of necrosis to a variable extent, similar to that seen in tuberculous osteomyelitis (Fig. 7).

- **Reactive osteitis:** Reactive (contiguous) osteitis occurs as a consequence of deep destruction of overlying soft tissues. Occasionally, the bone is exposed to the point of devascularization, necrosis of cortical bone, sequestration, and osteomyelitis. The macroscopic appearance is then that of white dead bone of almost normal appearance and texture.
Complications and sequelae

- **Contractures**
  Contractures result from scarring caused by lesions over or close to joints (Fig. 8a–b). Ankyloses may follow.

- **Bleeding**
  There may be continuous minor bleeding or a sudden major haemorrhage. Care should be taken to avoid large blood vessels beneath a lesion.

- **Secondary infection**
  Secondary bacterial infection may be caused by organisms such as staphylococci, streptococci, Pseudomonas sp., Corynebacterium sp., etc. Secondary infection may progress to cellulitis and septicaemia.

- **Extension to deep structures**
  Infection may extend beneath the deep fascia to involve tendon sheaths, muscle, blood vessels, nerves, bone and joints or may destroy periorbital tissue with loss of the eye.
Other sequelae

Hypertrophic scars and keloids may develop at infection and surgical sites including skin graft donor sites (Fig. 9). Squamous cell carcinoma (Marjolin’s ulcer) may appear in an unstable scar or persistent ulcer many years after initial infection with M. ulcerans. (Fig. 10).
5 Differential diagnosis

The differential diagnosis of nodules is more difficult than that of ulcers. Some common differential diagnoses are described in Buruli Ulcer: Mycobacterium ulcerans infection (ref. WHO/CDS/CPE/GBUI/2000.1). Table 1 and figures 11a and 11b relate to differential diagnosis.

![Figure 11a](Leishmaniasis)

![Figure 11b](Tropical phagedenic ulcer)

### Table 1

<table>
<thead>
<tr>
<th>Papule</th>
<th>Nodule</th>
<th>Plaque</th>
<th>Oedema</th>
<th>Ulcer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insect bites</td>
<td>Cyst</td>
<td>Leprosy</td>
<td>Cellulitis</td>
<td>Tropical phagedenic ulcer</td>
</tr>
<tr>
<td>Pimple</td>
<td>Lipoma</td>
<td>Cellulitis</td>
<td>Elephantiasis</td>
<td>Venous ulcer</td>
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<tr>
<td>Herpes</td>
<td>Onchocercoma</td>
<td>Mycosis</td>
<td>Actinomycosis</td>
<td>Leishmaniasis</td>
</tr>
<tr>
<td>Granuloma annulare</td>
<td>Boil</td>
<td>Psoriasis</td>
<td>Necrotizing fasciitis</td>
<td>Neurogenic ulcer</td>
</tr>
<tr>
<td>Psoriasis</td>
<td>Lymphadenitis</td>
<td>Haematomata</td>
<td>Osteomyelitis</td>
<td>Yaws</td>
</tr>
<tr>
<td>Pityriasis</td>
<td>Mycosis</td>
<td>Insect bites</td>
<td>Onchocercoma</td>
<td>Squamous cell carcinoma</td>
</tr>
</tbody>
</table>

**Note:** Infection caused by other mycobacterial organisms can be mistaken for any of the above.

*Table 1* Differential diagnoses of various forms of Buruli ulcer
Key points

1) Buruli ulcer disease presents as: papules, nodules, plaques, oedematous forms, ulcers and bone infections.
2) Contractures are easier to prevent than to correct.
3) Osteomyelitis may arise when an ulcer invades bone or when infection is blood-borne.

Notes
Plan of management

Collection of specimens | Types of specimens | Storage and transport of specimens | Assessment of the patient
Non-surgical treatment | Referral: levels of care

Chapter 2
Plan of management

**Objectives** This chapter will assist you to confirm your diagnosis and to develop a plan for managing your patient.

**Laboratory confirmation of diagnosis**

For further details of laboratory methods for the diagnosis of Mycobacterium ulcerans disease, refer to the companion manual dealing with laboratory methods for the diagnosis of this disease.

Tissue specimens (swabs or biopsies) from the lesion are examined by the following methods:

a) Ziehl-Neelsen (ZN) stain
b) Culture
c) Histopathology
d) Polymerase chain reaction (PCR)
Collection of specimens

It is important to prevent cross-contamination of specimens by the use of separate sterile or disposable instruments. Careful permanent labelling of specimen containers is essential. Never write directly onto the container. Write on an adhesive label.

Materials

• Sterile swabs—preferably cotton wool-tipped wooden swabs.
• Containers for fresh tissue specimens (no formalin or other preservatives) (Fig. 12).
• Containers for formalin fixation (10% formalin).
• Specimen containers of appropriate sizes are required for tissue fragments obtained from surgical procedures (e.g. sterile tubes for small specimens, sterile containers for large excisional specimens).

Types of specimens

• Non-ulcerative forms

Specimens for laboratory confirmation from non-ulcerative forms (i.e. papules, nodules, plaques and oedematous forms—see Chapter 1) should be taken from the centre of the surgically excised tissue and should include the entire thickness of clinically-infected tissue.

Especially for non-ulcerative plaques and oedematous forms, the patient or the patient’s relative should be asked to indicate the site at which the lesion first appeared, as this is the most likely site to yield a positive diagnosis but several further biopsies should be taken from other parts of the lesion. Tissue fragments from the periphery of a lesion are not recommended for microbiological studies, because *M. ulcerans* is often not found here but such specimens may be most suitable for histopathology.
• **Ulcerative forms**
  Multiple swabs should be taken from different sites, especially from beneath the undermined edges of lesions (Fig. 13).

  **Do not swab the slough in the centre of an ulcer.** Specimens that include all levels of the skin and subcutaneous tissue are most suitable for histopathological study.

• **Bone**
  Diagnostic procedures to assess bone involvement should only be performed at centres providing intermediate and high-level services. For amputation specimens, the involved bone or curetted samples are required; when amputation is not necessary, curetted bone samples are appropriate.
3 **Storage and transport of specimens**

**Sample to be stored** for immediate analysis—place in a sterile container without any additives.

**Sample to be transported:**
- Analysis within 24 hours—keep the sample cool (ideally at 4°C), e.g. in an insulated container with a frozen cooling block.
- Analysis after 24 hours (specimens may still be culture-positive up to 21 days):
  - when refrigeration facilities are available, keep at 4°C—do not freeze;
  - when refrigeration facilities are not available, transport medium is essential. Liquid Middlebrook 7H9 broth supplemented with polymyxin B, amphotericin B, nalidixic acid, trimethoprim and azlocillin (PANTA) is recommended. Supplementation with 0.5% agar achieves a semi-solid medium.

**Transport for PCR analysis**
PCR is best performed directly on fresh tissue specimens prepared as described above. For ulcerative forms, dry cotton wool swabs stored in their plastic containers at ambient temperature are acceptable.

4 **Assessment of the patient**
A general assessment should include assessment of nutritional state, weight, height, colour of mucous membranes and recognition of any coexisting diseases.

- **Laboratory tests**
  Routine investigations are haemoglobin (Hb), blood group and sickling test (where indicated). In the presence of super-added infection, send a wound swab for ordinary culture and antimicrobial susceptibility testing.
• **Radiological investigation**
  In cases where bone involvement is suspected, radiological investigation is appropriate (Fig. 14).

![Figure 14 X-ray of bone involvement in Buruli ulcer. See Figure 7 for physical presentation](image)

• **Assessment of the Mycobacterium ulcerans disease**
  Record the type of lesion (see Chapter 1), the site, the extent and the presence or absence of super-added infection and of any other complications. You should complete form BU 01 as described in Chapter 8. This should ensure systematic record keeping for every patient and should assist follow-up after discharge.
Non-surgical treatment

Although surgery is the mainstay of the treatment of *M. ulcerans* disease, there are occasions, especially in the presence of super-added infection, when an ulcer should be cleaned and dressed for a week or more before surgery. Elevation of an affected limb and splinting are important (see Chapter 7).

When there is secondary bacterial infection, start broad-spectrum antibiotic therapy by administering antibiotics such as combinations of penicillin, gentamicin and metronidazole. For some oedematous lesions, it is important to administer an antibiotic combination for 7–10 days prior to surgery.

Referral: levels of care

- **Level 1 - Peripheral or local community services**
  Cases should be identified, dressings applied and, where applicable, limbs should be immobilized in a position of function to prevent deformities and to allow comfortable transfer.

- **Level 2 - Basic surgical services**
  At the district hospital level, excision of nodules, papules, plaques and ulcers as well as skin grafting are appropriately performed by doctors and other trained health care providers. Note, depending on the capacity and expertise at the particular hospital, it may also be appropriate to perform some specialized surgery, e.g. amputation of limbs.

- **Level 3 - Specialized surgical services**
  Patients with severe extensive lesions and osteo-articular complications and other disabling sequelae should be referred for specialized surgery.

Criteria for referral. The criteria for referral of patients to level 2 and 3 services include:

- all ulcers > 2 cm;
- all oedematous and plaque forms;
- lesions involving deeper structures including bone;
- lesions on the head and neck, genitalia, breast and fingers;
- difficult diagnoses (clinically and by laboratory methods);
- systemically unwell patients.
Key points

1) Specimens for laboratory diagnosis of non-ulcerative forms should be taken from the centre of the surgically excised tissue.

2) Specimens for laboratory diagnosis of ulcerative forms should be taken from the undermined edges of the ulcer.

3) Make sure transported tissue specimens are not frozen.

Notes
Chapter 3

Anaesthetic assessment | Anaesthetic agents | Analgesia
Anaesthesia and analgesia

Objectives This chapter aims to assist the anaesthetic management of your patients.

The choice of anaesthesia may depend on the:

- Anaesthetist’s experience
- Available equipment and drugs
- Age of the patient
- Size and location of the lesion
- Patient’s preference
- Expected duration of surgery

Anaesthetic assessment

All patients should be thoroughly assessed to determine their suitability for local and/or general anaesthesia. The choice of anaesthesia will depend on the anaesthetist’s training and experience, available equipment and drugs, age of the patient (children may not cooperate with local anaesthesia), size and location of the lesion, patient preference and expected duration of the surgery.

The patient’s condition should be stable prior to surgery. Preoperative preparation should be directed to the patient’s general condition and the area to be operated upon. Appropriate laboratory tests should be ordered (see Chapter 2). Preoperative preparation must include a detailed explanation of the surgery to be performed and discussion of the potential complications and risks associated with the surgery. **A signed consent form detailing the risks of the surgery must be obtained before any premedication or surgical treatment.**
2 Anaesthetic agents
Premedication should be offered when indicated. Drugs administered can include morphine, pethidine, diazepam, midazolam, and promethazine.
Commonly used local anaesthetic agents include: lignocaine/lidocaine and bupivicaine with or without epinephrine/adrenaline. Local anaesthesia is used for smaller lesions, either by local injection or field blocks.
Never inject the anaesthetic agent directly into infected tissue. This is to avoid dissemination of M. ulcerans organisms. Mark the edges of the lesion, then inject around the lesion, not into it. Epinephrine reduces bleeding, but must not be injected into the hand or foot. Regional anaesthetic blocks or spinal anaesthesia are appropriate in the presence of large lesions, otherwise general anaesthesia will be necessary. Some of the general anaesthetic agents commonly used are: ketamine, isofloruane, fluothane, and ether. A ketamine/atropine cocktail, with diazepam or midazolam, is an effective way to sedate patients—especially children. Patients must be monitored continuously for airway, breathing and heart rate. Oxygen saturation should also be monitored if the equipment to do so is available. Careful observation of the patient during the early post-operative period is also of critical importance (ABC’s).
For upper and lower extremity lesions, tourniquets should be applied to minimize bleeding during surgery. Do not apply a tourniquet over a lesion. Do not leave a tourniquet in place for longer than two hours. Exsanguinate affected limbs by elevation alone.

3 Analgesia
Pain may be a serious issue throughout all stages of M. ulcerans disease. Mild pain may be relieved by simple agents such as paracetamol and non-steroidal anti-inflammatory agents (e.g. ibuprofen).
More severe pain may require narcotics. General anaesthesia may be required for some dressing changes.
Key points

1) Never inject local anaesthetic directly into an infected tissue.
2) Do not apply a tourniquet over a lesion.
3) Do not leave a tourniquet in place for longer than two hours.
4) Exsanguinate affected limbs by elevation alone.
5) Obtain written consent from patients.

Notes
Surgical treatment

Non-ulcerative forms | Ulcerative forms | Split-skin grafting technique | Complications and sequelae | Involvement of bone | Amputation

Chapter 4
Surgical treatment

Objectives This chapter will assist you to perform simple operations and to choose which patients to refer for specialized management.

Antibiotics Currently, surgery is the only proven effective treatment for M. ulcerans disease. Combination antibiotic therapy targeting M. ulcerans may be a beneficial adjunct to surgery. Note: its efficacy is not proven.

Antibiotics may be necessary to control super-infection. These agents may be chosen on the basis of disease presentation and the practitioner’s experience. Antibiotic therapy should be subsequently tailored according to culture and sensitivity results.

Non-ulcerative forms

- Papule: The procedure is the same as for a nodule. Depending upon the location of the lesion, the wound may be difficult to close by suture. If the wound edges cannot be brought together without undue tension, it is better to stop the bleeding and to leave the wound open.

A split-skin graft should then be applied at a later date. Otherwise, the wound should be dressed and the patient referred to hospital.
• **Nodules** should be excised only by appropriately trained health care providers. You must remove a nodule with a clear margin of normal tissue (Fig. 15a–d). The line of excision should be parallel to any nearby joint flexion crease. Remember to send a sample of the excised tissue for laboratory examination. Depending on the location, some lesions may be excised and the wound closed primarily by suture without undue tension. Large surgical wounds require split-skin grafting. Sutures are removed at 7 to 14 days, depending on the location of the wound and the progress of healing.

![Figure 15a](image1) Nodule
![Figure 15b](image2) Excision of a nodule
![Figure 15c](image3) Suturing
![Figure 15d](image4) Suturing

• **Plaque:** This is a more serious form of the disease which requires extensive excision (Fig. 16a–c) followed by split-skin grafting. Skin grafting over a flexion crease necessitates post-operative splinting and subsequent therapy to minimize flexion contracture.

![Figure 16a](image5) Plaque
![Figure 16b](image6) Developing plaque
![Figure 16c](image7) Excision of a plaque with limited excision of healthy tissue
**Surgical treatment**

The plane of excision usually spares deep fascia but, in some advanced cases extending deep to the fascia, the excision may include deep fascia and even muscle. Wherever possible, a pneumatic tourniquet is applied—but not for longer than two hours.

• **Oedematous form:** This form of the disease is complex. Urgent referral to a specialized centre is mandatory. Initial management should include elevation of the affected limb. At the specialist centre, an exploratory incision is made along the long axis of the oedematous area followed by blunt dissection of the affected tissue to reduce bleeding (Fig. 17a–d). Electro-cautery is an effective way of reducing blood loss.

![Figure 17a](image1.png) Incision marked – oedematous form

![Figure 17b](image2.png) Incision – oedematous form

![Figure 17c](image3.png) Dissection – oedematous form

![Figure 17d](image4.png) Completed excision

The plane of excision usually spares deep fascia but, in some advanced cases extending deep to the fascia, the excision may include deep fascia and even muscle. Wherever possible, a pneumatic tourniquet is applied—but not for longer than two hours.
2 Ulcerative forms

The surgical treatment of small ulcerative lesions is the same as that for nodules and papules (Fig. 18a). Larger lesions require excision (sometimes in stages) and split-skin grafting (Fig. 18b-d). Apply a pneumatic tourniquet whenever possible. Prior to surgery, secondarily infected lesions should be dressed, affected limbs elevated and appropriate antibiotics administered.

- **Technique of excision**
  
The required excision may be extensive. Large lesions may require staged excision, one area at a time. The excision must include healthy tissue at the lateral and deep margins. The deep fascia should be preserved if not involved but involved deep fascia must be removed, taking care not to open tendon sheaths or joints and not to damage important nerves and blood vessels. When diseased tissues have not been removed adequately, repeated excisions may be necessary. It is recommended that extensive lesions should be treated only at level two and level three services.
3 Split-skin grafting technique

Skin for grafting may be harvested using a razor or scalpel blade (Fig. 19), a Humby type knife or an electric dermatome.

The usually preferred sites for harvesting split-skin include the external aspect of the thigh and upper arm, the buttocks, the internal and external aspects of the forearm and the external aspect of the lower leg (in some instances, experienced surgeons choose split-skin graft donor sites that are later less visible).

To lessen friction, lubricate the intended donor site with a little sterile vaseline or liquid paraffin. Stretch the skin of the donor site by means of a metal plate at each end. Take thin split-skin grafts to allow donor-site healing within 21 days. Keep the skin graft moist with normal saline at all times.

To cover large areas, split-skin grafts may be expanded, preferably using a skin graft expander which does not require expensive disposable components.
Surgical treatment

Split-skin grafts may be secured at their edges and junctions using sutures or staples. Suture fixation of all full thickness skin grafts is advised. Vaseline gauze is applied, then a further thick absorbent dressing and a bandage.

Materials which may be used to make splints include: plaster of Paris for brief immobilization, aluminium, wood (which may be carved), fibreglass, and polyvinylchloride (PVC).

An alternative for the lower and upper limbs is suspension with slings and cords (Fig. 20), thus maintaining the joints in appropriate positions during the post-operative period.

Remove the surgical dressings on the third or fourth post-operative day unless there is haematoma or infection. Thereafter, change the dressings daily or on alternate days.

As soon as the graft has taken (at about 10 days post-operatively) commence mobilization.

To prevent joints from becoming stiff, limbs are best splinted with their joints in the following positions:
- knee in extension
- ankle at a right angle
- elbow in extension
- wrist in extension
- metacarpo-phalangeal joints in flexion
- interphalangeal joints in extension
Complications and sequelae

Complications such as contractures and loss of body parts, for example, the eye, ear, nose, and breast, always necessitate early referral to a major hospital for surgery and reconstruction. Specialist teams may visit district or local hospital services to provide treatment, such as the release of contractures. **Contractures should be released only as far as is safe, taking into account tension on blood vessels and nerves.** Skin defects are then covered by grafts or flaps, including musculo-cutaneous and muscle flaps.

- **The genitalia**
  Involvement of the genitalia constitutes a serious complication requiring immediate referral for specialized attention (Fig. 21).

- **The eye**
  After cleaning and dressing, eyelid and eye involvement necessitate urgent referral to a specialized centre (Fig. 22a and 22b).
The face, neck and breast

After the initial management, patients with lesions on the face, neck and breast must be referred to a specialized centre (Fig. 23, 24, 25).
5 Involvement of bone

Bone involvement occurs by direct extension from a surface lesion into the bone or an adjacent joint or as osteomyelitis. Patients with bone involvement must be referred immediately to a specialized centre.

• Surgical treatment of osteomyelitis

At operation, a limited exposure of the swelling and/or fistula track suffices for drainage of the abscess and for debridement of the gelatinous infected tissue. Extensive excision is not often required but, in some instances, definitive excision of infected soft tissues may be indicated. Post-operatively (Fig. 26a), the wound may be irrigated with antiseptic solutions (Fig. 26b).

A drain is inserted and the wound is partially closed but, at times, an experienced surgeon will close the wound to prevent secondary infection. If present, an open wound should be dressed regularly until satisfactory granulation tissue develops and split-skin grafting can be performed. Granulating wounds can be sequentially grafted as areas become clean enough for grafting.
Localized epiphyseal lesions (e.g. lesions involving the femoral condyles, the tibial plateau and the small bones of the hand and foot) often require repeated partial removal of involved bone in order to preserve the adjacent articular structures. The application of splints, plaster of Paris casts with windows or external fixation is essential to support the bone and thus to prevent pathological fractures—without interfering with wound care. X-rays at four to six weekly intervals are recommended to follow bone healing.

**Surgical treatment of reactive osteitis**

Reactive osteitis is a much less serious condition which should be treated conservatively. As retaining hypertrophied periosteum protects the underlying bone, debridement over bone is best limited to curettage, preserving as much periosteum as possible. Daily dressings lessen the risk of progression of bone involvement and promote the growth of granulations.

Necrotic cortical bone should be removed only after it has fully demarcated, as manifested by the growth of granulation tissue around and beneath it. Excessive bone removal must be avoided.

The ulcer may be excised and then partially grafted while awaiting separation of devitalized cortical bone. Grafting is completed after removal of the sequestrum. In the meanwhile, immobilization in the preferred position guards against pathological fractures and later contractures.

“To avoid unnecessary amputations, do not expose or remove bone widely.”
• **External fixation**

When there is extensive or circumferential tissue loss over a joint (e.g. elbow, wrist, knee, ankle), external fixation is applied at the time of the first procedure to keep the joints in the best possible position for function (Fig. 27). As noted above, external fixation facilitates dressings. External fixation is removed when healing is complete.
Amputation

Amputation should only be performed when reconstructive measures are impossible or have failed. It is rarely necessary. Ordinarily, the decision to amputate a limb should be taken in consultation with a specialist but severe uncontrollable bleeding may, occasionally, constitute a sufficient indication for an immediate life saving amputation. Steps for amputation are illustrated in figure 28.

“Amputation should only be performed when reconstructive measures are impossible or have failed. It is rarely necessary”.

Other clear indications for amputation include:
– completion of a necrotic auto-amputation;
– septicaemia/gangrene that would be life threatening without amputation;
– destruction of the function of a foot;
– extensive bone destruction.
**What you should not do!**

1. Do not prolong dressing regimens when excision is appropriate.
2. Do not rush to immediate excision.
3. Avoid prolonged non-specific antibiotic therapy.
4. Do not rely on specific antibiotics alone.
5. Do not perform incisional or punch biopsy of a small lesion. Excisional biopsy is preferable.
6. Do not infiltrate a local anaesthetic into any lesion.
7. Do not apply an Esmarch bandage over a lesion. Exsanguinate the limb by elevation alone.
8. Do not allow excessive blood loss (use a pneumatic tourniquet wherever possible).
9. Do not rely on curettage alone (except for osteomyelitis or when major structures are involved).
10. Do not count on spontaneous healing.
11. Do not burn your patient (after autoclaving remember to cool your instruments before use, especially your graft mesher).
12. Do not cover possibly infected tissue with a skin flap (flap cover requires special training).

**Key points**

1. All excisions must include a margin of healthy tissue.
2. Sutures should be removed only when the wound has securely healed.
3. Contractures always need early referral to a major hospital.
4. Exsanguinate affected limbs by elevation alone.
Nursing care

Chapter 5

General principles  Pre-operative wound care  Psychosocial support and education
Nursing care

General principles

Certified/registered nurses, other trained health care providers and family members provide nursing care. Professional nursing care, when available, involves the overall assessment of the patient and his or her family and socioeconomic environment. In places where patients often consult traditional healers, the dangers of some traditional treatments should be tactfully explained to the patients and their families.

Depending upon the level of services available, a nurse will need to decide whether to treat or to refer a patient. Nursing care should be provided before, during, and after surgery and may include rehabilitation services. A sympathetic, welcoming reception encourages and comforts the patient and family and thus, improves compliance and outcome. The patient should be fully informed concerning the treatment plan. Nurses should explain the necessity of taking the medication as prescribed and should confirm compliance.

Attention should be directed to the patient’s diet and personal hygiene. Any nutritional plan should take into account cultural practices and dietary habits. Where specific arrangements are available, register malnourished patients for supplementary nutrition. Where such arrangements are not available, encourage the family to prepare nutritious foods including local nuts and grains, eggs, fish and meat. Occasionally, when it is available, feeding of high calorie/high protein fluid through a nasogastric tube may be indicated.

Measures must be taken to prevent cross-infection, especially by HIV and hepatitis B/C viruses. Gloves should be worn while dressing wounds and must be replaced with a clean set between patients. If they are re-used, gloves must be cleaned and sterilized. Clean single-use disposable gloves, however, need not be sterilized prior to use. A new set of sterile instruments must be used for each patient.

For reasons of economy, where dressings are not readily available, re-use of bandages and even some dressing materials may be unavoidable. Bandages and dressings to be re-used are best rinsed in a washing machine. Bleach should then be added. Washing should be at a temperature of 90°C for one hour. The washed materials are then dried and sterilized.
In health facilities without washing machines, bandages and dressings should be placed in an antiseptic solution for at least one hour before washing by hand. Patients’ relatives responsible for washing bandages and dressings should be educated about how to handle the infected materials safely. The patient’s mattress should be protected by plastic sheeting. The bedsheets should be changed daily.

Pre-operative wound care

A complete shower/bath with clean water and soap is recommended before surgical procedures and dressing changes. Dressings may be removed under a shower or with water which has been boiled and cooled. The wound should then be washed and new dressings applied. Sterile gauze moistened with saline or an antiseptic solution such as hypochlorite, providone iodine or 2% acetic acid may be used. A 50/50 mixture of liquid paraffin and providone iodine at the time of dressing application will ensure a moist dressing and ease of removal—thus lessening bleeding. Several layers of gauze or other absorbent material may be necessary to adequately absorb the fluid exudate. Cover the dressing with a clean bandage. Dressings should be changed frequently—depending upon the amount of discharge from the wound or as advised by the surgeon. An infected wound needs to be dressed more frequently than a clean wound. Remember to consider oral and parenteral analgesia and, in some cases, general anaesthesia before dressing wounds (see Chapter 3).
Psychosocial support and education
Mycobacterium ulcerans disease may be devastating for patients and their families. Reassure the patient and family and offer advice about available social services. Educate patients and their families about the disease and about the need for early diagnosis and treatment.

“Mycobacterium ulcerans disease may be devastating for the patient and the family. Talk to the patient and family, reassure them and offer advice about available social services”.
Care in the community

Chapter 6

Dressing wounds | Village outreach activities | Extension of specialist services and training | Follow-up | Recurrence

Credit: WHO
Dressing wounds

Wash the wound with soap and drinking quality tap water or, where this is not available, water that has been boiled for 15 minutes and then cooled. In some places, community/village health care providers may be trained to dress simple wounds. For other more serious lesions, the wound should be cleaned and dressed and the person then referred to a district hospital.
2 **Village outreach activities**

Organize meetings with community elders and chiefs. Using aids such as educational materials, drama, videos and posters, explain the nature of the disease and stress that it is treatable (Fig. 29).

Encourage infected individuals to seek early treatment. Discussion of prognosis and rehabilitation may also be appropriate (see Chapter 7).

3 **Extension of specialist services and training**

Arrange for specialists from a main hospital to visit local communities and district hospitals to help manage your cases (Fig. 30). Which cases may be handled at this level will depend on the capacity at your facility. Health care providers may be trained during these visits. Find out about this from your hospital!
4 Follow-up
Follow-up of patients for several years via outreach visits to villages and hospital outpatient clinics greatly assists in a better understanding of the disease. These visits are designed to monitor treatment outcomes, for example, the development of scar contractures. Children should be followed up to assess the growth of grafts which may not keep up with the growth of normal tissues.

Key points
1) Encourage persons with Buruli ulcer to seek early treatment.
2) Educational materials should be organized with input from community elders and chiefs.

5 Recurrence
Follow-up entails watching for recurrence of infection and for the development of secondary deformities. Patients with recurrence or disability should be referred early for specialist treatment.
Rehabilitation

Chapter 7

Physiotherapy | Special devices | Occupational therapy and vocational retraining
Preventing stigmatization | Education and other assistance

Credit: WHO
Rehabilitation

Objectives

This chapter will assist you to understand the importance and essential features of rehabilitation for patients who have undergone surgery for Buruli ulcer.

Physiotherapy

The physiotherapist or a health care provider with special training should teach patients and their families how to position a limb to prevent deformities, how to exercise affected joints, and how to use special devices (mostly splints) when they are needed.

• Positioning

After surgery, a splint is often applied to hold a limb in a position that is good for function. The splint may be made of plaster of Paris, papier-mâché, plastic or wood. A pillow may be bandaged to a limb to hold it straight. After the wound has become stable (which may be before healing is complete), the patient should begin to move the limb, but it may be best to apply a splint at night to prevent a contracture. The surgeon will advise.

• Exercises

Passive exercise means that the limb is moved without contraction of its own muscles by the patient, physiotherapist or health care provider. This type of exercise commences as soon as the positioning splint is removed, while the patient is too weak or has too much pain to move the limb without help. The physiotherapist or health care provider should commence movement slowly and gently to avoid excessive pain and stretching of healing tissues.

Active exercise means that the patient moves the limb by contracting the limb’s own muscles. This becomes easier as strength improves and pain lessens. Later, exercises using weights, such as bags filled with rice, beans and/or sand are appropriate.
If a prosthesis (artificial limb – Fig. 32) or an orthosis (brace, calliper or splint – Fig. 34) is necessary, the surgeon or the physiotherapist or health care provider will refer the patient to a centre where the required appliance is made.

If a limb has been amputated, the physiotherapist should teach the patient how to exercise the retained part and how to bandage the stump so that it assumes a shape that fits well into an artificial limb. Proper training to use the prosthesis or orthosis is absolutely essential.

Patients not needing (or awaiting) an artificial limb or calliper who have difficulty walking after surgery may need assistance to use a cane or crutches (Fig. 31).

Patients with hand deformities may find self-care difficult. A physiotherapist or an occupational therapist may fashion special devices which help to hold objects such as cups, spoons and combs (Fig. 33).
Prostheses

• **Limb prostheses (artificial limbs)**
  Services to provide limb prostheses (artificial limbs) exist in most countries but often only in major cities. Therefore, these services are often difficult to access from rural and remote areas. Find out where the services are available in your area and the procedures for accessing them.

Before referring a person to a prosthetic/orthotic centre, start as early as possible to prepare for the fitting of a prosthesis by initiating exercises to ensure that there are no contractures. Bandage the stump to achieve a satisfactory conical shape (see above).

Once the wound has healed, the stump is no longer swollen and the limb has no (or minimal) contractures, the person should be referred to the centre where the required artificial limb will be made. An impression of the stump is first taken. Trials of the semi-finished prosthesis follow and training in the use of the new limb should then commence. This normally takes 2–3 weeks but the time taken varies greatly. Much encouragement is needed and many adjustments to the prosthesis are often required.

After the patient has returned to his/her community, continued support from the health care provider is essential. The patient often needs to return to the specialist centre for adjustment of the artificial limb.

• **Eye prostheses**
  These prostheses are individually made using an impression taken from the affected area. This service may not be available in your area.

“It is far easier to prevent a contracture than to correct it.”
Orthoses
An orthosis is a device which supports a weakened limb or keeps a limb in a chosen position. Orthoses are referred to as splints, braces or callipers. They are sometimes needed after surgical treatment. Advice should be obtained from an orthopaedic centre. Making an orthosis is often similar to making a prosthesis.

Occupational therapy and vocational retraining
The physiotherapist or health care provider should advise persons whose disabilities interfere with their work where to go for appropriate training, which may involve the use of special devices.

Preventing stigmatization
In countries where people suffer rejection because of physical deformities, explain to the patient and family that others will not catch the disease and that the patient needs their help to recover and to become active again. A community leader may be able to help the person gain acceptance and thus involvement in social activities and work.
5 Education and other assistance
Admission to hospital may provide an opportunity to commence or to recommence educational courses. Arrangements should be made with the education sector to ensure that children’s schooling continues during hospitalization (Fig. 35). Agencies may support social rehabilitation (e.g. financial assistance or support to set up a small business).

Figure 35
Education during hospitalization

“Admission to hospital may provide an opportunity to commence or to recommence educational courses”.

Notes
Recommendations for audit and research

Chapter 8
Recommendations for audit and research

This chapter deals with forms for recording and reporting Mycobacterium ulcerans disease to assist in data collection for research.

Record keeping using form BU 01
Form BU 01 (see Annex 9) should be completed for every patient to record demographic characteristics, risk factors, locations of lesions, clinical forms of the disease, laboratory confirmation, treatments and outcomes. This may be useful for clinical audit. Instructions to help you complete this form and diskettes to help you analyze your data may be obtained from:

The Global Buruli Ulcer Initiative, Communicable Diseases
World Health Organization
20, avenue Appia
CH-1211 Geneva 27, Switzerland

Implementation of the guidelines in this manual
These guidelines may be supported by locally-produced educational materials and workshops.

Indicators

Outcome indicators: average duration of stay in hospital; average treatment costs; recurrence rate; complications and sequelae rate; case fatality rate.

Clinical audit markers: compliance with guidelines in this manual; referral rate to specialized treatment and rehabilitation centres.

The following areas need action:
- care provision models (static versus mobile outreach services, community-based detection and referral activities)*
- implementation of these guidelines,
- time between patient arrival and first surgery* 
- management of various forms of the disease* 

* An economic evaluation should be included
Annexes

Noma  I  Prevention of HIV transmission  I  Blood transfusion and safety  I  Lists of equipment
Work of WHO on Buruli ulcer  I  Some research institutions involved in Buruli ulcer activities  I  Some NGOs and others involved in Buruli ulcer activities  I  Members of WHO Advisory Group on Buruli ulcer  I  Buruli ulcer form (BU 01)
Noma, cancrum oris or orofacial gangrene
(from a paper by Marie-Hélène Leclercq, WHO Action Programme Against Noma)

Noma is a serious disease of the mouth and face, of unknown etiology, which is associated with poverty and deprivation, especially poor nutrition and sanitation (Fig. 36a–c). Noma presently occurs in developing countries of all continents but previously occurred in Europe and elsewhere.

Children under six years of age are most commonly affected. The course of the disease is different from that of M. ulcerans but it is an important differential diagnosis.
Severe gingivitis is followed by rapidly extending ulceration within the mouth. The infection then spreads through the cheek which becomes oedematous and then necrotic. If septicaemia and death do not quickly supervene, a foul smelling purulent discharge precedes massive tissue loss and secondary healing by wound contracture. This often leads to distortion of the face with limitation of jaw motion.
Early treatment involves debridement, antibiotics (e.g. high dose penicillin) and improved nutrition. Subsequent restriction of opening of the jaw may be overcome by inserting sticks of various sizes between the teeth.
Severe deformities warrant more complex treatment including speech therapy. Cultural and social factors are highly relevant to treatment.
The WHO noma strategy involves early detection and treatment, education and training of health personnel, integration into health care services, epidemiology and etiological research and support of referral networks for surgical treatment and rehabilitation.
Prevention of HIV transmission

All body fluids from a person infected with HIV are potentially infectious. In this context, HIV may be transmitted by: (1) needles or sharp instruments contaminated with blood or body fluids; (2) contact between open wounds and broken skin (e.g. dermatitis), or mucous membranes contaminated by blood or body fluids; and (3) transfusion of infected blood or blood products, semen donation, and skin or organ transplantation.

Proper sterilization of all surgical instruments and supplies is crucial to preventing HIV transmission.

Several points are particularly relevant to the prevention of transmission of HIV:

- broken skin and open wounds should be protected with watertight dressings;
- gloves should be worn during exposure to blood or body fluids and the hands should be washed with soap and water afterwards; frequent use of ethanol or other antiseptics on the hands and arms should be avoided because it may lead to irritated broken skin;
- protective glasses should be worn when blood splashes may occur. If the eyes are inadvertently splashed, they should be washed out immediately with copious quantities of water.

All viruses, including HIV, are inactivated by steam sterilization (autoclaving) for 20 minutes at 100 kPa above atmospheric pressure or by heat treatment in an oven for 2 hours at 170°C.

Most of the small number of reported occupational infections of health workers with HIV have resulted from injury by needles (e.g. during recapping) and other sharp instruments. After use, disposable needles and scalpel blades should be put into a puncture-proof receptacle, preferably containing a sodium hypochlorite disinfectant. **Needles must never be reused.**

Surgical gloves protect against transmission of HIV, but there is always the possibility of a glove being punctured. Thick gloves should therefore be worn when sharp instruments are being cleaned. Where HIV infection is prevalent among patients, instruments should be routinely soaked in a chemical disinfectant for 30 minutes before cleaning. Linen soiled by a patient who is or may be infected with HIV should be handled with gloves and transported in leak-proof bags. It should be washed with detergent for 25 minutes at a temperature of at least 71°C (or soaked in a hypochlorite disinfectant before washing).

Liquid wastes should be carefully poured down a drain connected to a sewer or into a pit latrine or they should be chemically disinfected. Solid wastes should be incinerated or disposed of in a pit latrine; chemical disinfection may be a temporary expedient.
3 Blood transfusion and safety

**Blood donations**
- Voluntary unremunerated donors.
- Screening for blood-borne pathogens including HIV, hepatitis B and hepatitis C viruses (Fig. 37).
- Continuous supply of test kits throughout the year.

**Clinical uses of blood**
1) Blood and blood products should be used only for conditions with significant potential for morbidity or mortality and their need should be confirmed by careful assessment of clinical and laboratory indications.
2) Clinical assessment of anaemia should be based on examination of the tongue, palms, eyes and nailbed.
3) Laboratory assessment should be based on haemoglobin measurement, haematocrit or the haemoglobin colour scale (Fig. 38).
4) Transfusion may be needed before, during or after surgery. Plan carefully for the blood needs of the patient.
5) Before prescribing blood and blood products, consider the following:
• What are the specific indications for transfusion of this patient?
• What improvement in the patient’s condition am I looking for?
• Can I minimize blood loss to reduce the need for transfusion?

6) Correct procedures should always be followed for the ordering, administering and monitoring of transfusions. Finally, if in doubt, ask yourself: “If this blood were for myself or my relative, would I accept the transfusion under these circumstances?”

- Are there other treatments (e.g. intravenous fluids or oxygen) I should give before deciding to transfuse?
- What are the risks of transmitting HIV, hepatitis, syphilis or other blood infections? (Fig. 39)
- Do the benefits of transfusion outweigh the risks?
- What options are there if no blood is available in time?
- Will a trained person monitor this patient and respond immediately if an acute transfusion reaction occurs?
- Have I recorded my decision and the reasons for transfusion?
# Lists of equipment

Surgical trays and equipment for specific procedures.

This annex lists some of the instruments, equipment, and materials desirable for minor operations, including excision of nodules and skin grafting.

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</tr>
<tr>
<td>Small curved artery forceps, 3 pairs at least</td>
<td>Ruler</td>
</tr>
<tr>
<td>Small straight artery forceps, 3 pairs</td>
<td>Scalpel handle with No. 10 blade</td>
</tr>
<tr>
<td>Sponge forceps</td>
<td>Skin hooks, 4</td>
</tr>
<tr>
<td>Sterile drapes</td>
<td>Skin-grafting knife, and blade</td>
</tr>
<tr>
<td>Sterile gloves</td>
<td>Small, curved artery forceps, 6 pairs</td>
</tr>
<tr>
<td>Stitch scissors</td>
<td>Small, straight artery forceps, 6 pairs</td>
</tr>
<tr>
<td>Sutures, 2/0, 3/0, and 4/0 chronic catgut, with and without round bodied needles</td>
<td>Sponge forceps</td>
</tr>
<tr>
<td>Sutures, 2/0, 3/0, and 4/0 non-absorbable, with and without cutting needles</td>
<td>Sterile drapes</td>
</tr>
<tr>
<td>Syringe, 5 ml and 10 ml with needle</td>
<td>Sterile gloves</td>
</tr>
<tr>
<td>Tissue forceps</td>
<td>Stitch scissors</td>
</tr>
<tr>
<td>Towel clips, 4</td>
<td>Tissue forceps (Allis), 2 pairs</td>
</tr>
</tbody>
</table>

Towel clips, 4
Work of WHO on Buruli ulcer

On the advice of world experts, WHO has taken the leadership in coordinating Buruli ulcer control and research efforts worldwide. This is essential in order to maintain effective function and focus. WHO/GBUI activities since early 1998—when the Initiative was established—include the following:

1) A preliminary meeting of an ad hoc Task Force was held in February 1998. Later, an Advisory Committee of 18 experts was established. This Committee includes world authorities on Buruli ulcer and representatives from endemic countries. Some group members contributed to the recently published monograph and this manual.

2) The first International Conference on Buruli Ulcer Control and Research was held in Yamoussoukro, Côte d’Ivoire, 6–8 July 1998. This resulted in an increased awareness of the disease. At this Conference, the Yamoussoukro Declaration on Buruli ulcer was signed by three heads of state and the Director-General of WHO. The report of this Conference, in English and in French, is available for distribution.

3) Assessments in Benin, Côte d’Ivoire, Ghana, and Togo were conducted between March and July 1998 with the aim of understanding the problem of Buruli ulcer and discussing the importance of the disease with various government authorities. As a result, focused programmes have been established in Benin, Côte d’Ivoire, Ghana, Guinea, and Togo. More countries are establishing programmes.

4) Progress has been achieved in raising the awareness of the significance of Buruli ulcer. However, as the disease is still unknown to many, more work needs to be done. A newly established website (www.who.int/gtb-buruli) will assist to make available much needed information. The first WHO educational leaflets, in English and in French, targeting community workers at district and village levels, have been printed and distributed in endemic countries.

5) Standard case definitions and forms for the surveillance and clinical management of patients, as well as standard guidelines for treatment and referral of patients, have been developed by the WHO Advisory Committee in consultation with other experts worldwide.

6) A WHO scientific working group, consisting of some 40 world experts in the disease, known as the International Mycobacterium ulcerans Study Team (IMuST), has been established in collaboration with A/Prof. John Hayman, from the Monash University, Melbourne, Australia. The IMuST seeks to develop control and research activities, and to help coordinate the world’s efforts against Buruli ulcer.
7) Collaborating centres will be established in some international research institutions to support research and training activities.

8) Research in the following priority areas, which have the potential of impacting on the control of the disease, has been advised by the WHO Advisory Group and IMuST:
   - operational steps in the implementation of adequate control measures;
   - mode(s) of transmission;
   - environmental changes that favour emergence of the disease;
   - surveys to determine the burden of the disease;
   - chemical structure of the toxin;
   - rapid methods of diagnosis; and
   - action of known antimicrobial drugs on M. ulcerans, starting with animal models and continuing to clinical trials.
Some research institutions involved in Buruli ulcer activities

- Armed Forces Institute of Pathology (AFIP), Washington DC, USA
- Bactériologie et Hygiène, Faculté de Médecine Pitié-Salpêtrière, Paris, France
- Centers for Disease Control and Prevention (CDC), Atlanta, GA, USA
- Department of Anatomy and Cell Biology, Monash University, Melbourne, Australia
- Department of Infectious Diseases, Austin and Repatriation Medical Centre, Melbourne, Australia
- Department of Internal Medicine, University Hospital, Groningen, The Netherlands
- Department of Medicine, Emory University School of Medicine, Atlanta, GA, USA
- Department of Microbiology, Bernhard Nocht Institute for Tropical Medicine, Hamburg, Germany
- Department of Microbiology, Monash University, Victoria, Australia
- Department of Microbiology, University of Tennessee, Knoxville, TN, USA
- Institute of Tropical Medicine, Antwerp, Belgium
- Laboratoire de Bactériologie, Centre Hospitalier Universitaire d’Angers, Angers, France
- Microbiological Research Unit, Royal Children's Hospital, Melbourne, Australia
- Nagoya University, Graduate School of Medicine, Nagoya, Japan
- Nippon Medical School, Tokyo, Japan
- Noguchi Memorial Institute for Medical Research, Accra, Ghana
- Pasteur Institute of Guiana, Cayenne, French Guiana
- Plastic Surgery & Burns Center, Korle-Bu Teaching Hospital, Accra, Ghana
- St George’s Hospital Medical School, London, England
- Swiss Tropical Institute, Basel, Switzerland
- Unité Génétique Moléculaire Bactérienne, Pasteur Institute, Paris, France
Some nongovernmental organizations and others involved in Buruli ulcer activities

- Acción Sanitaria y Desarrollo Social (ANESVAD), Spain
- Aide aux Lépreux Emmaüs-Suisse (ALES), Switzerland
- American Leprosy Missions (ALM), USA
- Association Française Raoul Follereau (AFRF), France
- Associazione Italiana Amici di Raoul Follereau (AIFO), Italy
- Catriona Hargreaves Charitable Trust (CHCT), England
- Damien Foundation, Belgium
- Directorate General for International Cooperation, Belgium
- Fondation Luxembourgeoise Raoul Follereau (FFL), Luxembourg
- Government of Japan
- Humanitarian Aid Relief Team (HART), USA
- Japan Tissue Engineering Co., Ltd, Japan
- Kobe International University, Japan
- Médecins Sans Frontières (MSF), Luxembourg & Switzerland
- MAP International, West Africa, Côte d’Ivoire
- Pharmaciens Sans Frontières, France
- Projet Humanitaire Afrique Nord Sud (PHANS), France
- Pfizer Pharmaceuticals Inc., USA
- Rotary Club of Milan, Italy
- Sasakawa Memorial Health Foundation, Japan
- The Nippon Foundation, Japan
Members of the WHO Advisory Group on Buruli ulcer

- **Dr George Amofah**, Public Health Division, Ministry of Health, P. O. Box M-44, Accra, Ghana
- **Dr David Ashford**, Meningitis and Special Pathogens Branch, CDC, 1600 Clifton Rd, Atlanta, GA 30333, USA
- **Dr John Buntine**, Cornell Specialists’ Centre, 13 Cornell Street, Camberwell, Victoria, 3124, Australia
- **Prof. Jacques Grosset**, Bactériologie et Hygiène, Faculté de Médecine Pitié-Salpêtrière, 91, boulevard de l’Hôpital, 75634 Paris Cedex 13, France
- **Dr Augustin Guédénon**, Programme National de Lutte contre l’Ulcère de Buruli, Ministère de la Santé publique, 06 BP 2572, Cotonou, Benin
- **A/Prof. John Hayman**, Department of Anatomy and Cell Biology, Monash Univ., Clayton, Melbourne, 3800, Australia
- **A/Prof. Paul Johnson**, Department of Infectious Diseases, Austin and Repatriation Medical Centre, Heidelberg, 3084 Melbourne, Australia
- **Sister Joseph**, Wewak General Hospital, Private Mailbag, Wewak, East Sepik Province, Papua New Guinea
- **Prof. Jean-Marie Kanga**, Programme National de Lutte contre l’Ulcère de Buruli, 18 BP 2890, Abidjan 18, Côte d’Ivoire
- **Prof. Kenzo Kiikuni**, Sasakawa Memorial Health Foundation, 1-2-2 Akasaka, Minato-Ku, Tokyo 107-0052, Japan
- **Dr Harold King**, Division of Infectious Diseases, Department of Medicine, Emory School of Medicine, 69 Butler Street, S.E., Atlanta, GA 30303, USA
- **Dr Wayne M. Meyers**, Division of Microbiology, Armed Forces Institute of Pathology, Washington, DC, 20306-6000, USA
- **Prof. Françoise Portaels**, Department of Microbiology, Institute of Tropical Medicine, Nationalestraat 155, B-2000, Antwerp, Belgium
- **Dr Roger Pradinaud**, Service de Dermatologie, Centre hospitalier général de Cayenne, Cayenne Cedex, Guyane Française
- **Dr G. Battista Priuli**, Hôpital Saint-Jean-de-Dieu, BP 7, Tanguïéta, Benin
- **Dr Pamela L. Small**, Department of Microbiology, 409 Walters Life Sciences, University of Tennessee, Knoxville, TN 37996-0845, USA
- **Dr Napo Tignokpa**, Programme contre la Lèpre et la Tuberculose, Ministère de la Santé, BP 2271, Lomé, Togo
- **Dr Mark Wansbrough-Jones**, Division of Infectious Disease, St. George’s Hospital Medical School, Cranmer Terrace, London SW17 0RE, England
### A. Institutional information

1. Name of Institution, address
2. Sub-district ........ District ........ Region ........ Country ........
3. Name of Officer completing this form (Last/First)
4. Title .................................. Specialization ..................................

### B. Patient information

5. Health facility ID* ................................ Date of admission ....
6. Name (Last/First) ................................ 7. Age .............. 8. Sex  M ☐ F ☐
9. Address .................................................................
10. Sub-district ........ District ........ Region ........ Country ........
11. Occupation of patient ..............................................
12. Source of drinking water ☐ Pipe-borne ☐ Borehole/well ☐ River/stream ☐ Pond/stagnant
13. Patient classification ☐ New case ☐ Recurrent case ☐ Different site ☐ Same site
   Date of last treatment ..................................................
14. Duration of illness before seeking care .................... months
15. Use of traditional treatment ☐ N ☐ Y ☐
16. History of cases in family/among relatives ☐ N ☐ Y ☐
17. History of trauma or site of lesion ☐ N ☐ Y ☐
18. BCG vaccination or scar ☐ N ☐ Y ☐

### C. Location of lesion(s)

19. **Upper limbs:** Left ☐ Right ☐ **Lower limbs:** Left ☐ Right ☐ **Abdomen** ☐ **Back** ☐
   **Buttocks & perineum** ☐ **Thorax** ☐ **Head & Neck** ☐

* This form should be kept in the patient's record at the health facility where treatment is provided
### D. Clinical forms

<p>| | | | | | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Active</td>
<td>Nodule</td>
<td>Papule</td>
<td>Plaque</td>
<td>Oedema</td>
<td>Ulcer</td>
</tr>
<tr>
<td></td>
<td>Inactive</td>
<td>Scar due to Buruli ulcer</td>
<td>Amputation due to Buruli ulcer</td>
<td>Other</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

20. Disability present upon presentation: N Y

22. Date of clinical diagnosis (dd/mm/yy)

---

### E. Confirmation of clinical diagnosis

<table>
<thead>
<tr>
<th></th>
<th>ZN staining</th>
<th>Culture</th>
<th>PCR</th>
<th>Histopathology</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Positive</td>
<td>Positive</td>
<td>Positive</td>
<td>Positive</td>
</tr>
<tr>
<td></td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td></td>
<td>Not done</td>
<td>Not done</td>
<td>Not done</td>
<td>Not done</td>
</tr>
</tbody>
</table>

---

### F. Principal treatment(s)

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>24.</td>
<td>Wound dressing only</td>
<td>Excision only</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Amputation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Antimycobacterial agents, specify</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Antibiotics and other drugs</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Others</td>
</tr>
</tbody>
</table>

---

### G. Treatment outcomes

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>25.</td>
<td>Healed without sequelae</td>
<td>Healed with sequelae, specify</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Referral for treatment of active lesions: where</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Absconded/discharged against medical advice</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Died, Buruli ulcer related, specify</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Died, not related to Buruli ulcer, specify</td>
</tr>
</tbody>
</table>

---

### H. Referral of sequelae

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>26.</td>
<td>No, why not</td>
<td>Yes, where</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Date (dd/mm/yy)</td>
</tr>
</tbody>
</table>

27. Date of discharge (dd/mm/yy)
Available further materials

• Buruli ulcer (Mycobacterium ulcerans infection). WHO/CDS/CPE/GBUI/2000.1 (English, French, Spanish)
• Diagnosis of Mycobacterium ulcerans disease (Buruli ulcer). WHO/CDS/CPE/GBUI/2001.4 (English, French, Spanish)
• Buruli ulcer comic. WHO/CDS/CPE/GBUI/2001.5 (English, French)
• Brochure on Buruli ulcer. WHO/CDS/CPE/SMT/2001.6 (English, French, Spanish)
• Posters and leaflets on Buruli ulcer (English, French)
• 9 minutes 25 seconds video on Buruli ulcer (English, French, Spanish)
• Epi info software for data management (English, French)
• Training video—diagnosis and management of Buruli ulcer (English, French)

For more information, contact:

Global Buruli Ulcer Initiative
Communicable diseases
World Health Organization
1211 Geneva 27 – Switzerland
Tel. (41) 22 791 2803/2498
Fax (41) 22 791 4777
E-mail: Buruli@who.int
Internet: www.who.int/gtb-buruli
This manual provides an authoritative guide to the diagnosis and clinical management of Buruli ulcer, a mycobacterial disease that causes immense suffering and crippling deformities in a growing number of tropical countries. Addressed to district health care providers, the manual aims to facilitate a better understanding of this difficult disease, its clinical presentation, and its surgical management.

A comprehensive protocol, adapted to each form and stage of the disease, is presented together with comments on the levels of resources and capabilities needed to shorten the length of treatment, to prevent complications, and to minimize undesired sequelae, and thus to obtain the best possible outcome for each patient.

As surgical treatment is presently the definitive management strategy, the manual includes detailed information on specific surgical procedures for both non-ulcerative and ulcerative forms of the disease, and for complications and sequelae. Chapters on nursing care, care in the community, and rehabilitation are also included. Throughout, numerous colour photographs and line drawings are used to enhance the manual’s value as a training and reference tool.

Methods for the laboratory diagnosis of Mycobacterium ulcerans disease are covered in a companion volume, *Diagnosis of Mycobacterium ulcerans disease: A manual for health care providers.*